The Final Office Action

The Office has withdrawn its rejection of claims 1-3, 22, 24, and 26 under 35 U.S.C. § 112. The Office has maintained its rejection of claims 1-3 under 35 U.S.C. § 102(b) in view of Monti et al. (*PAACR Annual Meeting 36*:387, Abstract 2304 (March 1995)) ("Monti I"). The Office has maintained its rejection of claims 24-27 under 35 U.S.C. § 103(a) over Monti et al. (*PAACR Annual Meeting 38*:193, Abstract 1298 (March 1997)) ("Monti II") in view of Harris (*J. Nat'l Cancer Inst. 88*:1442-1455 (1996)) ("Harris"). Applicants request reconsideration of these rejections.

Discussion of the Rejection Under 35 U.S.C. § 102(b)

The Office has rejected claims 1-3 under Section 102(b) as allegedly being anticipated by Monti I. This rejection is traversed for the reasons set forth below.

According to the Office, claims 1-3 of the instant application are anticipated by Monti I because, allegedly, the claimed prophylactic use of nitroxides to prevent cancer in an animal is inherently disclosed by Monti I. Monti I summarily states that "Tempol ... was recently reported to act as radioprotector in mice." The Office contends that "[i]t is now well settled law that administrating compounds inherently possessing a protective utility anticipates claims directed to such protective use." (Office Action, page 4, second full paragraph). Despite the Office' contention that this is "well settled law," the Office cites no legal authority for this alleged precedent. Indeed, Applicants can find no law asserting such a broad expansion of the inherency doctrine.

Anticipation by inherency is a narrow doctrine with limited application. A reference is anticipatory only if it discloses every limitation of the claimed invention either explicitly or inherently. *Atlas Powder Co. v. Ireco Inc.*, 190 F.3d 1342, 1346, 51 USPQ2d 1943, 1945 (Fed. Cir. 1999). A reference includes an inherent characteristic if that characteristic is the "natural result" flowing from the reference's explicitly explicated limitations. *Continental Can Co. USA, Inc. v. Monsanto Co.*, 948 F.2d 1264, 1269, 20 USPQ2d 1746, 1749 (Fed. Cir. 1991) (citations omitted). To establish inherency, the Federal Circuit has held that "the extrinsic evidence must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill." *In re Robertson*, 169 F.3d 743, 745, 49 USPQ2d 1949, 1950 (Fed. Cir. 1999) (citations omitted). In other words, "the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art." *Ex parte Levy*,

17 USPQ2d 1461, 1464 (Bd. Pat. App. & Inter. 1990). In this case, it is clear that the Office has proffered no evidence that, in view of Monti I, the natural result flowing from administration of nitroxides is the prevention of cancer.

The fact that an agent may act as a radioprotector does not necessarily mean that the compound can be used to treat cancer prophylactically. All biological responses are the natural and inherent result of the chemical agent administered to the animal, whether or not the responses have been discovered. More is required to show anticipation by inherency. *Ex parte Levy*, 17 USPQ2d at 1464 (holding that the Examiner must provide factual or technical reasoning). Inherency may not be established by mere probabilities or possibilities. *Robertson*, 169 F.3d at 745, 49 USPQ2d at 1950-51. To establish inherency, "[t]he mere fact that a certain thing may result from a given set of circumstances is not sufficient." *Id.* In view of Monti I, the mere possibility or probability that radioprotectors may serve to prevent cancer is not sufficient to establish inherency.

While cancer is one possible result of exposure to radiation, the two are not mutually inclusive. It is well-known that exposure to radiation can lead to many disease states other than cancer (e.g., uterine myoma, chronic hepatitis, liver cirrhosis, cataracts, altered immune functions, circulatory disease, digestive disease, etc.) *See, e.g.*, Wong, et al., *Radiation Research, 135*, 418-430 (1993). Also, an animal may have cancer as a result of sources other than radiation, such as a genetic defect or exposure to a non-radioactive carcinogen. Gleaned from the Office's reasoning is that any compound capable of acting as a radioprotector necessarily acts to prevent these other disease states, e.g., cataracts and cancer caused by non-radioactive means, e.g., genetic defect. Clearly, the Office's reasoning is nothing more than mere conjecture. *See, e.g., W.L. Gore v. Garlock, Inc.*, 721 F.2d 1540, 1554, 220 USPQ 303, 314 (Fed. Cir. 1983) ("Anticipation ... cannot be predicated on mere conjecture respecting the characteristics of products that might result from the practice of processes disclosed in references.") Accordingly, the Office has failed to meet its burden of showing that Monti I anticipates claims 1-3 of the instant application under the narrow doctrine of anticipation by inherency.

Even assuming, for the sake of argument, that prevention of cancer does flow naturally from radioprotection, Monti I still does not anticipate claims 1-3 of the instant application because Monti I does not enable the invention. A reference cannot anticipate that which it does not enable. *In re Spada*, 911 F.2d 705, 708, 15 USPQ2d 1655, 1657 (Fed. Cir. 1990) (in order to anticipate, "the [prior art] reference must describe the applicant's claimed invention sufficiently to have placed a person of ordinary skill in the field of the invention in

possession of it"). The Office's reliance on *Ex parte Novitski* does not diminish the enablement requirement. In *Novitski*, the prior art reference fully enabled the invention claimed in the application rejected by the Office. 26 U.S.P.Q.2d 1389 (Bd. Pat. App. & Int. 1993) (concluding that if the authors of the prior art reference, *having taken the manipulative steps described in the reference* of inoculating plants with a particular bacteria, had then attempted to measure for the results described by the inventor of nematode inhibition, the authors of the prior art reference would have necessarily uncovered it) (emphasis added). Hence, in order to anticipate, Monti I must describe the claimed invention sufficiently to have placed a person of ordinary skill in the art in possession of the invention.

Monti's mere conclusory statement that Tempol has been found to act as a radioprotector in mice does not by itself teach or suggest, and hence does not enable, a method of using a nitroxide, or a prodrug thereof, for the prophylactic or therapeutic treatment of cancer in an animal. Monti I provides no teaching whatsoever regarding nitroxides in the prophylaxis of cancer, such as *in vivo* activity, suitable doses, formulation, modes of administration and types of cancer. Nor does Monti I provide a working example or any other experimental data regarding the effectiveness of nitroxides in the treatment of cancer in an animal. Absent these teachings, Monti I cannot anticipate claims 1-3 of the instant application. To conclude otherwise would require the Office to use the instant specification as a blue print to construct its anticipation rejection, resulting in an impermissible use of hindsight. *See, e.g., Rowe v. Dror*, 112 F.3d 473, 478, 480-81, 42 USPQ2d 1550, 1553, 1555 (Fed. Cir. 1997) (in regards to anticipation by inherency, "[a]bout the most that can be said for the [prior art] patent is that it does not explicitly describe anything inconsistent with [the claimed] procedures. However, this negative pregnant is not enough to show anticipation."); *In re Newell*, 891 F.2d 899, 13 USPQ2d 1248 (Fed. Cir. 1989) ("[A] retrospective view of inherency is not a substitute for some teaching or suggestion which supports the selection and use of the various elements in the particular claimed combination.")

In view of the above, Applicants submit that claims 1-3 are not anticipated by Monti I. Accordingly, Applicants request the withdrawal of this rejection.

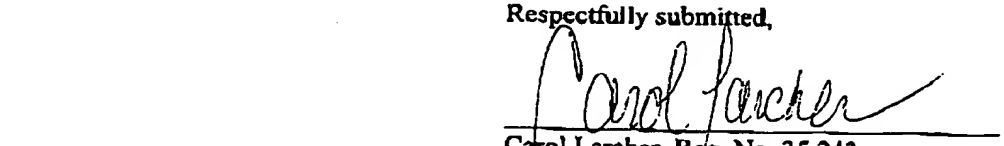
Discussion of the Rejection Under 35 U.S.C. § 103(a)

The Office has rejected claims 24-27 under Section 103(a) over Monti II in view of Harris. This rejection is traversed for the reasons set forth below.

Conclusion

The application is considered to be in good and proper form for allowance, and the Examiner is respectfully requested to pass this application to issue. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned attorney.

Respectfully submitted,



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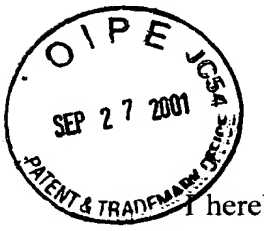
Monti II studied *in vitro* the mutagenic and cytotoxic effects of the Tempol against DNA repair-deficient bacterial strains. Monti II does nothing more than suggest that similar effects *might* be observed in an *in vitro* study of tumor cell lines. There is no teaching or suggestion in Monti II of a method of using a nitroxide, or a prodrug thereof, to treat cancer in an animal prophylactically or therapeutically as taught by the present invention. The Office attempts to cure the deficiencies of Monti II by alleging that "[i]t is old and well known in the art to employ an agent that is effective in vitro study into vivo study to monitor its efficacy." See, Office Action, page 5 (underlines original). In doing so, the Office has applied the wrong standard in assessing obviousness. That "monitoring the efficacy" of a compound *in vivo* may be old and well-known does not, in and of itself, constitute a teaching or suggestion to use a nitroxide (or a prodrug thereof) in the prophylactic and therapeutic treatment of cancer, particularly when the primary reference, itself, does not extrapolate from the effects observed for tumor cell lines *in vitro* to efficacy *in vivo*. Monti II simply does not motivate the ordinarily skilled artisan to use a nitroxide (or prodrug thereof) in the prophylactic or therapeutic treatment of cancer in an animal, let alone teach or suggest such a use. Monti II also does not provide an ordinarily skilled artisan with a reasonable expectation of success.

The Office's citation of Harris as a secondary reference does not cure the deficiencies of the primary reference Monti II. The Office relies on Harris's disclosure that many cancers are a result of p53 mutations. Yet, Harris states that promyelocytic HL-60 cells, the very cells utilized in the *in vitro* study in Monti II, are p53 null (page 9, line 23). It is also known in the art that myeloblastic KG1 cells, also used in the *in vitro* study in Monti II, are null for p53 expression as well. See Guillouf, et al., *Oncogene*, *10*(11), 2263-2270 (1995) and Shimizu, et al., *Exp. Cell Res. 226*(2), 292-301 (1996). Consequently, in contrast to the Office's allegation, one having ordinary skill in the art would not have been motivated to combine the teachings of Monti II and Harris. Even assuming, for the sake of argument, that one of ordinary skill in the art would have been motivated to make such a combination, which Applicants maintain is not the case, the ordinarily skilled artisan would have done nothing more than test tumor cell lines *in vitro*. Simply put, neither reference teaches or suggests the *in vivo* method taught by the present invention and neither reference provides a reasonable expectation of success in doing so.

In view of the above, Applicants submit that claims 24-27 are not obvious in view of Monti II and Harris. Accordingly, Applicants request the withdrawal of this rejection.

In re Appln. of Mitchell et al.
Application No. 09/424,519



CERTIFICATE OF MAILING

I hereby certify that this RESPONSE TO FINAL OFFICE ACTION (along with any documents referred to as being attached or enclosed) is being deposited with the United States Postal Service on the date shown below with sufficient postage as first class mail in an envelope addressed to: Assistant Commissioner for Patents, Box AF, Washington, D.C. 20231.

Date: September 24, 2001 Ellen K. Marcus

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